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# MAGNETIC NON-EQUIVALENCE IN THE LOW-TEMPERATURE NUCLEAR MAGNETIC RESONANCE SPECTRA OF N-BENZYL- N-METHYLHYDROXYL- AMINE AND ITS ANION— COMPARISON WITH SCF —MO CALCULATIONS

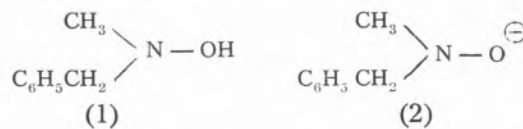
From the  $^1\text{H}$  n.m.r. analysis of N-benzyl-N-methylhydroxylamine and its anion the observed magnetic non-equivalence of the benzylic protons is rationalised in terms of slow nitrogen inversion being the rate determining step in the dynamic process. Molecular orbital calculations (MNDO and *ab initio*) carried out on the model N,N-dimethylhydroxylamine and the corresponding anion lend further support to this hypothesis.

## INTRODUCTION

The conformational analysis of compounds containing single bonds between atoms bearing pairs of nonbonding electrons have attracted considerable attention, [1] including hydroxylamine and its derivatives.

Since the observation of magnetic non-equivalence in the low-temperature  $^1\text{H}$  n.m.r. spectra of some hydroxylamines derivatives, there has been controversy concerning the nature of the measured rate process. Whereas in the case of cyclic hydroxylamines there seems to exist general agreement as to the origin of the observed magnetic non-equivalence, which is attributed to pyramidal inversion at N, [2-4] the opposite holds for acyclic hydroxylamines. In the latter case a competitive intramolecular conformational process leading to a substantial barrier to rotation about the N-O bond cannot be dismissed *a priori*.

Previous work [5] had shown that N-benzyl-N-methylhydroxylamine does exhibit magnetic non-equivalence of the benzylic hydrogens at low temperature.



It is the aim of our work to contribute to the clarification of the factors involved in the observed magnetic non-equivalence of the methylene group in the low temperature  $^1\text{H}$  n.m.r. spectra of N-benzyl-N-methylhydroxylamine 1 and its anionic derivative 2.

## RESULTS AND DISCUSSION

$^1\text{H}$ . n.m.r. analysis. — At room temperature (probe temperature at  $300 \pm 3$  K) and in  $\text{CD}_3\text{OD}$ , the  $^1\text{H}$  n.m.r. spectra of 1 (see Table 1) showed, for the two benzylic protons, a sharp singlet at  $\delta$  3.85, while its corresponding anion showed for the same methylene group a broad absorption at ca.

$\delta$  3.73 (see Table 1). The upfield shift can be accounted for by the shielding effect of the adjacent negative oxygen.

On lowering the temperature, the signals due to the methylene protons of (1) and (2) broadened, and finally became AB quartets (see Table 2), the temperature of coalescence being approximately 266 and 289 K

observed in the anion is noteworthy. For this kind of compound this can only be rationalised by the larger anisochrony resulting from a different orientation of the benzylic protons and the lone pair in the nitrogen atom of 2, relative to 1. We also note that the broadening as a function of temperature was fully reversible, indicating that broadening

Table 1

$^1\text{H}$  N.M.R. data at  $300 \pm 3$  K

Compound	Solvent	$\delta$ * (number of protons, multiplicity **)		
		$\text{CH}_3$	$\text{CH}_2$	Ar-H
$\text{PhCH}_2\text{NMeOH}$	$\text{CD}_3\text{OD}$	2.61 (3, s)	3.85 (2, s)	7.30-7.32 (5, m)
$\text{PhCH}_2\text{NMeO}^\ominus \text{Na}^\oplus$	$\text{CD}_3\text{OD}$	2.47 (3, s)	3.73 (2, b)	7.20-7.34 (5, m)

\* p.p.m. from T.M.S.

\*\* s = singlet, b = broad singlet, m = multiplet.

for the neutral and charged species respectively.

The limit of exchange broadening was approximately 220 K for 1, while for the corresponding anion no significant changes were observed below 238 K. The much larger difference between the chemical shifts of the diastereoisotopic protons (anisochrony)

due to the presence of paramagnetic impurities from oxidation of the hydroxylamine can be discounted.

The rate constants of chemical exchange at different temperatures were determined by lineshape analysis of the AB quartets. These were obtained by visual comparison between the experimental spectrum and the com-

Table 2

Low temperature  $^1\text{H}$  n.m.r. data for the methylene protons

Compound *	$\Delta\nu_{\text{AB}}/\text{Hz}$	$J_{\text{AE}}/\text{Hz}$	$T_c/\text{K}$
$\text{PhCH}_2\text{NMeOH}$ (219.8 K)	31.29	— 12.67	265.8
$\text{PhCH}_2\text{NMeO}^\ominus \text{Na}^\oplus$ (238.2 K)	137.82	— 11.65	287.9

\* In brackets the temperature below which no further changes in lineshape could be observed.

puted line shape for the hydroxylamine and its anion (see Fig. 1 and Fig. 2).

Kinetic data with the corresponding Eyring parameters can be found in Table 3 and 4,

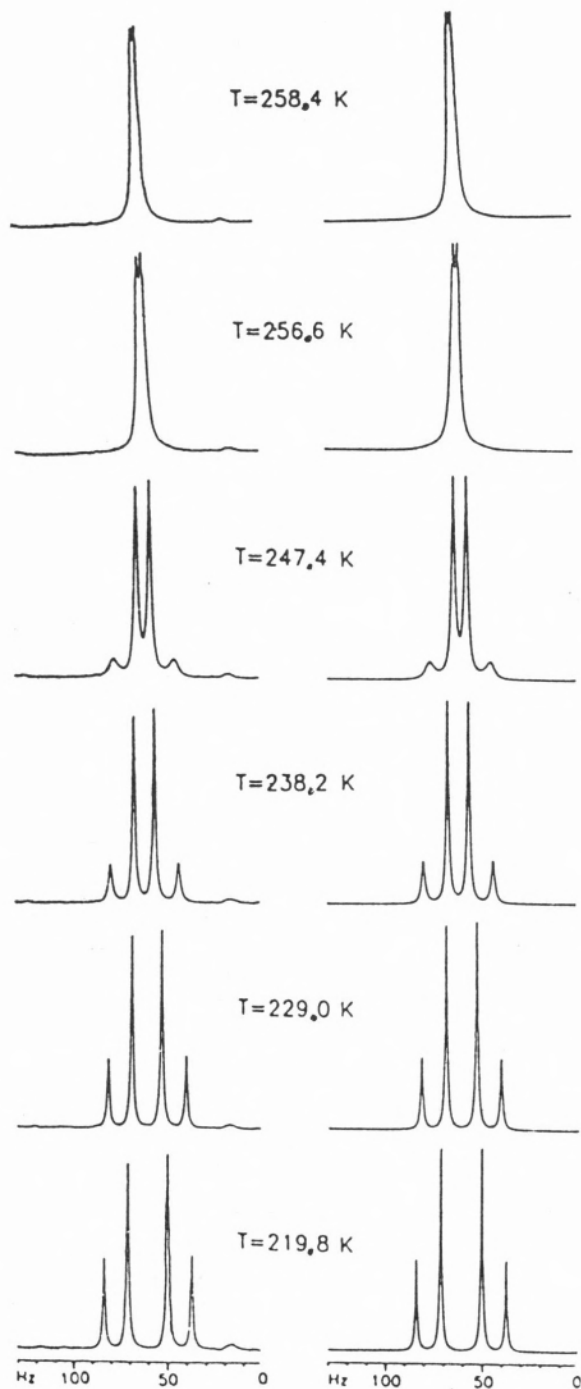


Fig. 1

Experimental (left) and computed (right) d.n.m.r. spectra of  $\text{PhCH}_2\text{NMeOH}$ .

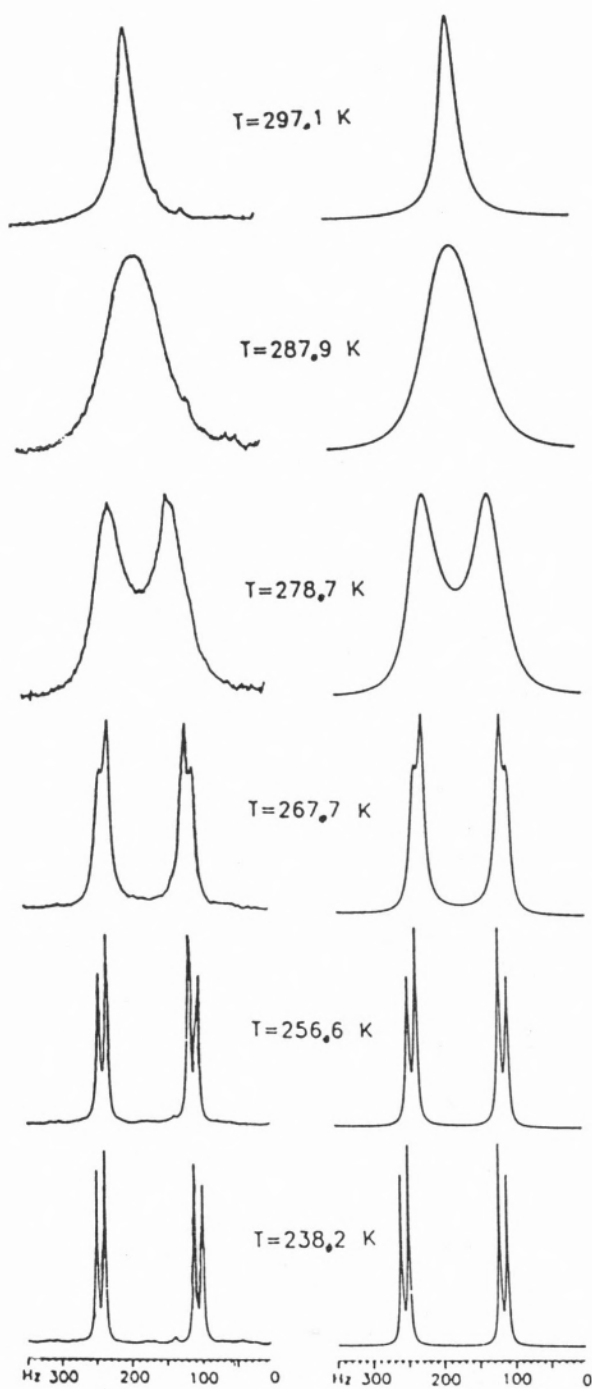


Fig. 2

Experimental (left) and computed (right) d.n.m.r. spectra of  $\text{PhCH}_2\text{NMeO}^\ominus\text{Na}^\oplus$ .

Table 3

Kinetic data for  $\text{PhCH}_2\text{NCH}_3\text{OH}$   
 ( $\sim 0.02 \text{ M}$  in  $\text{CD}_3\text{OD}$ ;  $T_2 = 0.25 \text{ s}$ )

Temperature K	$k/\text{s}^{-1}$	$\Delta\nu/\text{Hz}$	$10^3 (1/T)/\text{K}^{-1}$	$\ln (k/T)$
229.0	0.5	25.5	4.367	— 6.126
238.2	2.0	19.9	4.198	— 4.780
247.4	8.0	15.3	4.042	— 3.432
256.6	26.6	12.0	3.897	— 2.267
258.4	32.0	10.0	3.870	— 2.089

Table 4

Kinetic data for  $\text{PhCH}_2\text{NCH}_3\text{O}^\ominus\text{Na}^\oplus$   
 ( $\sim 0.02 \text{ M}$  in  $\text{CD}_3\text{OD}/\text{CD}_3\text{O}^\ominus\text{Na}^\oplus$ ;  $T_2 = 0.15 \text{ s}$ )

Temperature K	$k/\text{s}^{-1}$	$\Delta\nu/\text{Hz}$	$10^3 (1/T)/\text{K}^{-1}$	$\ln (k/T)$
256.6	9.5	128.0	3.897	— 3.244
267.7	29.5	120.2	3.736	— 2.009
278.7	136.0	114.1	3.588	— 0.881
287.9	296.0	108.7	3.473	— 0.004
297.1	660.0	103.2	3.365	0.818

while the Eyring plots are shown in Fig. 3 and 4 respectively.

The activation parameters displayed in Table 5 indicate:

1 — A good agreement between the value of  $\Delta G^\ddagger$  ( $53.6 \text{ kJ mol}^{-1}$ ) for **1** in deuterated methanol and the reported [5] value ( $51.9 \text{ kJ mol}^{-1}$ ) in deuterated acetone.

2 — The free energy of activation for the anion **2**, relative to **1** is only marginally higher, ( $2.9 \text{ kJ mol}^{-1}$ ), lending support to the importance of electronic differences. In **2**, there are three lone pairs on the oxygen, resulting in greater repulsion with the nitrogen lone pair in the transition state. Furthermore in **2**, magnetic nonequivalence must arise as the result of slow nitrogen inversion, because the angle of rotation about the N-O bond remains undefined.

As pointed out earlier, [5] the steric acceleration found for *N*-benzyl-*N*,*O*-dimethylhydroxylamine ( $\Delta G_c^\ddagger$  41.4 kJ mol<sup>-1</sup> in ace-

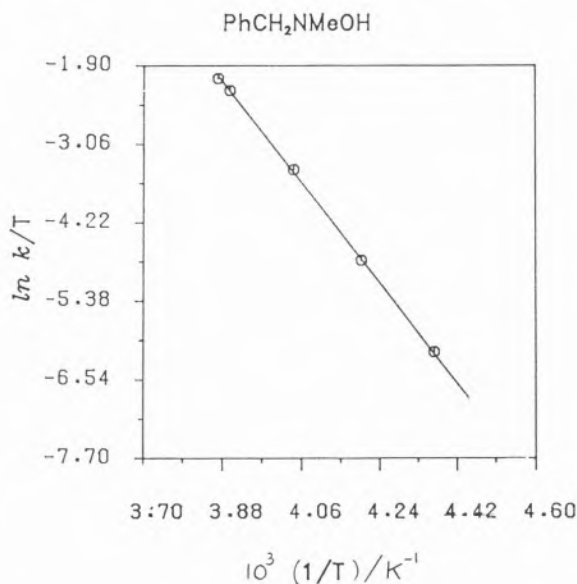


Fig. 3

Eyring plot for PhCH<sub>2</sub>NMeOH.

tone-d<sub>6</sub>) relative to *N*-benzyl-*N*-methylhydroxylamine ( $\Delta G_c^\ddagger$  51.9 kJ mol<sup>-1</sup> in the same

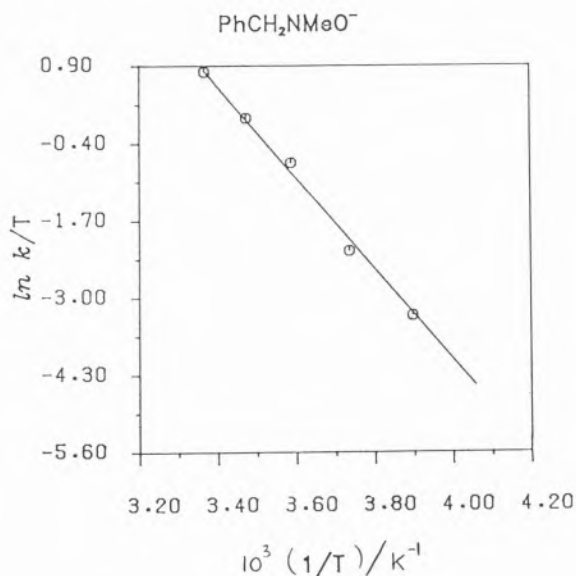
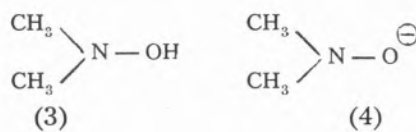


Fig. 4

Eyring plot for PhCH<sub>2</sub>NMeO<sup>-</sup>Na<sup>+</sup>

solvent) has been taken to confirm likewise that nitrogen inversion is the rate determining step of the dynamic process associated with the diastereotopicity of the methylene protons. A similar conclusion was reached by Hall [7] and his group, studying various *N*-arylethyl-*N*,*O*-dimethylhydroxylamines, but increase in the bulkiness of the groups attached to *N* and *O* can dramatically change this situation as found more recently by Iwamura [8] and coworkers. The Japanese chemists, who assigned the slow step to restricted rotation around one of the skeletal C - N - O - C bonds, based their conclusion on the fact that practically no change in the energetic barriers were found when a benzyl group attached to nitrogen was replaced by a phenyl in a similar hydroxylamine derivative. In our hands however, *N*-benzyl-*N*-phenylhydroxylamine failed to show any magnetic non-equivalence of the methylene protons when the temperature was as low as 190 K.

**SCF - MO Calculations**—The results of molecular orbital calculations, by the MNDO [14] and *ab initio* [15] methods using a STO-3G basis set, carried out on the models *N*, *N*-dimethylhydroxylamine 3 and the corresponding anion 4 are summarised in Table 6.



A generally greater value of  $\Delta G_c^\ddagger$  was found for the anionic derivative 4 than for the neutral molecule 3, the differences being however bigger in the theoretical calculations, ( $\Delta \Delta G_c^\ddagger$  37.7 kJ mol<sup>-1</sup>—MNDO; 13.6 kJ mol<sup>-1</sup>—STO-3G // MNDO) than in the actual result ( $\Delta \Delta G_c^\ddagger$  2.9 kJ mol<sup>-1</sup>). A better agreement with experimental values is thus found when using the STO-3G // MNDO method.

A smaller theoretical value for the activation entropy is found for the anion relative

Table 5

Coalescence temperature and activation parameters for N-benzyl-N-methylhydroxylamine and its anion

Compound	Solvent	$T_c/K$	$\Delta H^\ddagger/kJ\ mol^{-1}$	$\Delta S^\ddagger/JK^{-1}\ mol^{-1}$	$\Delta G_{298}^\ddagger/kJ\ mol^{-1}$
PhCH <sub>2</sub> NMeOH	CD <sub>3</sub> OD	265.8	$68.2 \pm 2.9$	$49.0 \pm 0.8$	$53.6 \pm 2.9$
PhCH <sub>2</sub> NMeO <sup>⊖</sup> Na <sup>⊕</sup>	CD <sub>3</sub> OD	287.9	$65.7 \pm 10.0$	$36.5 \pm 2.9$	$56.5 \pm 10.0$

Table 6

Molecular orbital calculations for the nitrogen inversion of N,N-dimethylhydroxylamine and its anion

	$\Delta H^\ddagger$ (method) KJ mol <sup>-1</sup>	$\Delta S^\ddagger$ (method) JK <sup>-1</sup> ml <sup>-1</sup>	$\Delta G_{298}^\ddagger$ (method) KJ mol <sup>-1</sup>
Me <sub>2</sub> NHOH	31.1 (a) (MNDO) 60.3 (b) (STO-3G // MNDO)	12.3 (MNDO) —	27.4 (MNDO) 58.8 (c) (STO-3G // MNDO)
Me <sub>2</sub> NHO <sup>⊖</sup> Na <sup>⊕</sup>	65.6 (a) (MNDO) 72.9 (b) (STO-3G // MNDO)	1.8 (MNDO) —	65.1 (MNDO) 72.4 (c) (STO-3G // MNDO)

(a) Difference between the transition and ground state heat of formation.

(b) Difference between the transition and ground state absolute energy.

(c) MNDO values were used to calculate  $\Delta G^\ddagger$ :

to the neutral hydroxylamine ( $\Delta\Delta S^\ddagger$  10.5 Jk<sup>-1</sup> mol<sup>-1</sup>), which is nevertheless less than the experimental difference ( $\Delta\Delta S^\ddagger$  18.4 Jk<sup>-1</sup> mol<sup>-1</sup>). However the fact that  $\Delta S^\ddagger$  is the parameter most dependent on errors in the lineshape analysis would limit the weight of any theoretical interpretation advanced.

## CONCLUSIONS

Given the good theoretical concordance found with the experimental results obtained, and the similarity of the values of the free energy of activation for the dynamic processes occurring with 3 and 4, the best rationale for the origin of the rate-limiting process governing the non-equivalence of the

an aqueous solution of N-methylhydroxylamine group in both 1 and 2 is slow-nitrogen inversion. This process is in any case the only conceivable explanation for the behaviour presented by 2.

The slightly greater value for the free energy of activation observed for the anion can be explained in terms of an increase in instability experienced by its nitrogen planar transition state, due to a greater repulsive effect between the electronic nitrogen lone pair and the negative charge in the oxygen atom.

## EXPERIMENTAL

### N-Methylbenzaldoxime

To a suspension of benzaldehyde (2.6 g) in 2 N sodium hydroxide (70 cm<sup>3</sup>) was added



an aqueous solution of *N*-methylhydroxylamine (2.2 g in 5 cm<sup>3</sup>). T.l.c. control showed that, after 1 hour of stirring at room temperature, all the aldehyde had disappeared, and the *N*-methylbenzaldoxime, remaining in solution, was extracted several times with dichloromethane (3 × 10 cm<sup>3</sup>). The organic phase was dried with magnesium sulfate, the solvent was evaporated under reduced pressure, giving rise to a solid residue. On crystallisation from benzene-*n*-hexane white crystals (3.13 g, 94 %) of *N*-methylbenzaldoxime were obtained with m.p. 83-84° (lit. [9] 84°).

#### *N*-Methyl-*N*-benzylhydroxylamine

A solution of *N*-methylbenzaldoxime (3.04 g) in a mixture of benzene (10 cm<sup>3</sup>) and ether (30 cm<sup>3</sup>) was added to a suspension of lithium hydride (0.45 g) in ether (10 cm<sup>3</sup>) and the mixture refluxed for 4 hours.

The reaction mixture was treated with a small amount of water (ca. 2 cm<sup>3</sup>), the white inorganic precipitate filtered off and extracted with diethyl ether (3 × 10 cm<sup>3</sup>).

The combined extracts were dried with anhydrous sodium sulfate, the organic solution was concentrated under reduced pressure and the residue recrystallised from *n*-hexane to give *N*-methyl-*N*-benzylhydroxylamine (2.83 g, 98 %), m.p. 40-41° lit. [10] 40-41°.

#### *N*-Methyl-*N*-benzylhydroxylamine anion

To solution of *N*-methyl-*N*-benzylhydroxylamine in CD<sub>3</sub>OD was added carefully with stirring an excess of sodium metal.

#### <sup>1</sup>H N.M.R. Spectroscopy

Spectra were recorded on a Brüker WM 250 spectrometer and the sample temperature calibrated using a standard methanol sample together with the chemical shift data of Van Geet [11].

The lineshape analysis of the *AB* spin system corresponding to the diastereoisotopic methylene protons of the *N*-benzyl group was carried out by comparison with simulated spectra produced by the program DNMR 3H [12].

The temperature dependence of the resonance frequency differences  $\Delta\nu_{AB}$  is displayed on Tables 3 & 4. In regions where exchange broadening prevented direct measurement of  $\Delta\nu_{AB}$  these parameters were obtained by least square extrapolation from lower temperature values. The coupling constants  $J_{AB}$  were found to be temperature independent. The rate constant  $k$  for the exchange process and the spin-spin relaxation time  $T_2$  were adjusted to produce the best visual fit. The latter values did not differ significantly from those obtained from the low temperature limiting spectra

$$(T_2 = \frac{1}{\pi \omega_{1/2}}).$$

Activation parameters for the *AB* exchange process were obtained by a least square analysis of the rate constants as a function of temperature using the Eyring equation [13].

#### SCF — MO Calculations

Molecular orbital calculations of the activation enthalpy,  $\Delta H^\ddagger$  for the *N*-inversion of 3 and 4, were carried out using the MNDO [14] method with full geometry optimisation and the *ab initio* method (basis set STO-3G) [15], at the optimised MNDO geometry (STO-3G // MNDO).

Activation enthalpies for 3 and 4 were obtained by difference between the transition state (*N* planar) and the ground state (optimized geometry) enthalpies of formation (MNDO) or absolute energies (STO-3G // MNDO).

Activation entropies were obtained from the difference between the calculated molar entropy of the ground state and the planar

transition state, using the method described previously, [16] and the calculated MNDO normal vibrational frequencies [17].

To reduce the computation time, the benzyl groups of 1 and 2 were modelled by methyl groups.

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## RESUMO

Da análise de  $^1\text{H}$  r.m.n. da N-benzil-N-metil-hidroxilamina e seu anião, a não-equivalência magnética observada nos prótons benzílicos é racionalizada em termos de ser a inversão lenta do átomo de azoto o passo determinante da velocidade do processo dinâmico. Cálculos de orbitais moleculares (MNDO e ab initio) levados a cabo no composto modelo N,N-dimetil-hidroxilamina e respectivo anião emprestam suporte adicional a esta hipótese,